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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ANDERSON, REBECCA L	
ART UNIT	**PAPER NUMBER**
1626	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,845	IIDA ET AL.	
	Examiner	Art Unit	
	REBECCA L. ANDERSON	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-76* is/are pending in the application.

4a) Of the above claim(s) *2-7,10-15,19-24,30,32,35-39,43-46,53,55 and 62-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8,9,16-18,25-29,31,33,34,40-42,47-52,54,56-61 and 68-76* is/are rejected.

7)☒ Claim(s) *1,8,9,16-18,25-29,31,33,34,40-42,47-52,54,56-61 and 68-76* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/26/08, 6/29/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

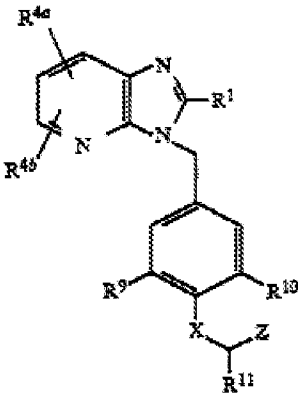
DETAILED ACTION

Claims 1-76 are currently pending in the instant application. Claims 1, 8, 9, 16-18, 25-29, 31, 33, 34, 40-42, 47-52, 54, 56-61 and 68-76 are objected and rejected. Claims 2-7, 10-15, 19-24, 30, 32, 35-39, 43-46, 53, 55 and 62-67 are withdrawn from consideration as being for non-elected subject matter.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-61 and 68-76 and the further election of the compound 127 in the reply filed on 26 April 2010 is acknowledged.

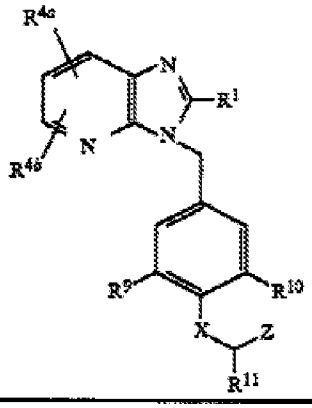
Applicants' elected species of compound 127 is not allowable as can be seen by the following 35 USC 112 1st and 2nd paragraph rejections. However, in order to expedite prosecution, according to MPEP 803.02, the search and examination of the claims has been extended the non-elected species of the compound:



wherein X is NMe, R1 is Et, R4a is 4-Me, R4b is 7-Me, R9 is H, R10 is H, R11 is Ph and Z is COOH, which is not allowable.

Claims 1, 8, 9, 16-18, 25-29, 31, 33, 34, 40-42, 47-52, 54, 56-61 and 68-76 **have been examined to the extent that they are readable on the elected embodiment,**

the elected species compound 127 and the non-elected species:



wherein X is NMe, R1 is Et, R4a is 4-Me, R4b is 7-Me, R9 is H, R10 is H, R11 is Ph and Z is COOH. Since the elected embodiment is not allowable, subject matter not embraced by the elected embodiment is therefore withdrawn from further consideration.

It has been determined that the entire scope claimed is not patentable

Drawings

The subject matter of this application admits of illustration by a drawing to facilitate understanding of the invention. Applicant is required to furnish a drawing under 37 CFR 1.81(c). No new matter may be introduced in the required drawing. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). Specifically, pages 116-119 discuss Figures 1-4, but no figures are found in the instant application.

Specification

The disclosure is objected to because of the following: Pages 116-119 refer to figures 1-4 which are not found in the instant application.

Appropriate correction is required.

Claim Objections

Claims 1, 8, 9, 16-18, 25-29, 31, 33, 34, 40-42, 47-52, 54, 56-61 and 68-76 are objected to as containing non-elected subject matter. Claims 1, 8, 9, 16-18, 25-29, 31, 33, 34, 40-42, 47-52, 54, 56-61 and 68-76 presented drawn solely to the elected embodiment identified supra would overcome this objection, as would an amendment to overcome the pending rejections of the claims as the examiner would then extend the search according to MPEP 803.02.

Claims 9, 16, 17, 27, 34, 40-42 and 50 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to claims in the alternative. The reference found in the claims to definitions as "described above" is referring to multiple claims. For example, claim 9, which is written as an “independent” claim, is an improper multiple dependent claim as it defines, for example, W1, as T described above, but T is described above in claims 1, 3, 5, 6 and 7. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 34 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the provisos of the claim are unclear as there is

no "if" "then" or "when" "then" language present. Therefore the claim is unclear as it is not known what is provided out, for example the phrase:

"Provided that Z2 is a nitrogen atom, R35 is a hydrogen atom or lower alkyl, R36 and R37 are each a hydrogen atom, lower alkyl, or an aliphatic heterocyclic group, and R34 is lower alkoxy or halogen-substituted lower alkoxy, W2 is not –OR12a…"

could be interpreted as "if Z2 is a nitrogen atom, then R35 is a hydrogen atom…" which would mean that any time Z2 is nitrogen, the R35 must be a hydrogen. The phrase could also be interpreted as "if Z2 is a nitrogen atom, R35 is a hydrogen atom or lower alkyl and R36 and R37 are each a hydrogen atom, lower alkyl, or an aliphatic heterocyclic group, then R34 is lower alkoxy or halogen-substitued lower alkoxy and W2 is not –OR12a", which means that if Z2, R35, R36 and R37 are as mentioned, then R34 is always a lower alkoxy or halogen-substituted lower alkoxy and W2 is not -OR12a. Other interpretations could also be present. Therefore, the claim is considered indefinite.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 68-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 68-76 provides for the use of the bicyclic heterocyclic compounds of claim 1, claim 9 or claim 34, but, since the claim does not set forth any steps involved in the

method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 68-76 are is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

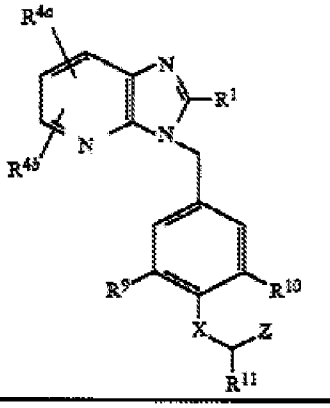
Claims 68-76 have been interpreted as products (i) compounds according to formulae (I), (II) or (III) as stated on page 2 of the restriction requirement mailed 24 March 2010.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8, 16-18, 25-29, 31, 54, 58-61 and 68, 70, 71, 73, 74 and 66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of neutrophilic asthma with the compound



wherein X is NMe, R1 is Et, R4a is 4-Me, R4b is 7-Me, R9 is H, R10 is H, R11 is Ph and Z is COOH does not reasonably provide enablement for the treatment of neutrophilic asthma with any other compound or for the treatment or prevention of any other disease derived form hyperfunction of GPR4 or any neutrophilic inflammatory disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The nature of the invention

The nature of the invention of claims 1, 8, 16-18, 25-29, 31, 54, 58-61 and 68, 70, 71, 73, 74 and 66 is products with the intended use of treating and/or preventing neutrophilic inflammatory diseases or diseases derived from hyperfunction of GPR4. Page 58 of the instant specification defines these diseases to include, for example, AIDS and certain cancers such as lung cancer and squamous cell carcinoma.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological

activities (i.e. what compounds can treat or prevent which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic and preventive effects of the above listed diseases, whether or not the disease is effected by the the mGluR5 receptor would make a difference.

Applicants are claiming products with intended uses which include the treatment or prevention of various diseases such as inflammation, certain cancers, AIDS, etc.

In regards to products for the treatment and prevention of inflammatory disorders, enablement for the scope of treating inflammatory disorders generally is not present. For a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process, which can take place individually in any part of the body. There is a vast range of forms that in can take, causes for the problem, and biochemical pathways that mediate the inflammatory

reaction. There is no common mechanism by which all, or even most, inflammations arise. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally. Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilation and leaking of vessels, and recruitment of circulating neurophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. There are clusters of macrophages, which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters. Otitis media is an inflammation of the lining of the middle ear and is commonly caused by Streptococcus pneumoniae and Haemophilus influenzae. Cystitis is an inflammation of the bladder, usually caused by bacteria, Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasoacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulites is inflammation of the tissues around the eye, and Orbital cellulites is an inflammatory process involving the

layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise form staphylococcus. Hence, these types of inflammations are treated with antibiotics. Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to accept any agent to be able to treat or prevent inflammation generally.

Applicants claims encompass products with the intended use of treatment or prevention of various cancers. The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531) Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91) that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may

be treated by selected NO-blocking drugs. These example shows that there are different cellular mechanisms, the unpredictability in the art and the different treatment protocols.

For example, Applicants are claiming products with the intended use of a method of treating or preventing AIDS. As such, the specification fails to enable the skilled artisan to use the compounds of the formula (I) to prevent or treat HIV. In addition, there is no proof that the claimed compounds have ever been administered to a human or to an animal model. The obstacles to therapeutic approaches and vaccine development with regard to retroviruses associated with AIDS in humans are well documented in the literature. See, for example, Huff {J. Med. Chem. 34(8) 1991, p. 2305-2314} on page 2314. These obstacles include and are not limited to: 1) the extensive genomic diversity associated with HIV, particularly with respect to the gene encoding the envelope protein, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a convert form, as well as via free virus transmission, 3) existence of a latent form of the virus, 4) the ability of the retrovirus to traverse the blood brain barrier and 5) the complexity and variation of the elaboration of the disease. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting therapeutic regimen on its face. In addition, there is no established correlation between in vitro activity and accomplishing treatment of viral infections, especially HIV infections, in vivo, and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and

those skilled in the art would not be able to use the compounds of the formula (I) since there is no description of an actual method wherein a viral infection in a host is treated or prevented.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment or prevention one of skill in the art is unable to fully predict possible results from the administration of the compounds claimed due to the unpredictability provided supra.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of diseases applicant considers as treatable and preventable on page 58 and assay data on pages 112-117. However, it is noted that the assay data on pages 112-117 refers to figures which are not present in the instant application. Additionally, there are no working examples present for the treatment or prevention of any specific disease or disorder. Additionally, the disclosure does not provide how the in vitro data correlates to the treatment of the assorted list of disorders of the instant claims.

Further, there is no disclosure regarding how all types of the diseases having divers mechanisms are treated or prevented. Receptor activity is generally unpredictable and a highly structure specific area, and the data provided of is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the claimed compounds can treat or prevent the extremely difficult diseases embraced by the instant claims.

There is also no disclosure as to how the various types of inflammatory disorders are treated or prevented.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.” See In re

Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is for products with the intended use of treating and/or preventing neutrophilic inflammatory diseases or diseases derived from hyperfunction of GPR4. Page 58 of the instant specification defines these diseases to include, for example, AIDS and certain cancers such as lung cancer and squamous cell carcinoma.

The disorders encompassed by the instant claims include, for example, inflammatory diseases some of which have been proven to be extremely difficult to treat. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of all diseases would be benefited (treated or prevented) and would furthermore then have to determine which of the claimed compounds would provide treatment of which disease, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which

diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims for the treatment or prevention of diseases claimed as a result necessitating one of skill to perform an exhaustive search for which diseases can be treated or prevented by what compounds of the instant claims in order to practice the claimed invention. (Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not mean that the other diseases meet the enablement requirements).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated or prevented by

the compound encompassed in the instant claims, with no assurance of success. Applicant could overcome this objection by deleting the intended use from the product claims.

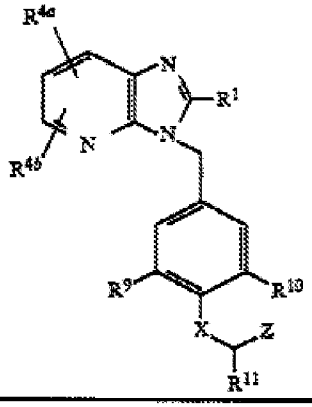
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8, 9, 16, 25-29, 31, 33, 34, 40, 48-52, 54, 56-61 and 68-76 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,374,638.

U.S. Patent No. 5,374,638 discloses products of the formula I (column 3) which are useful for treating asthma (column 2). A particular compound:



wherein X is NMe, R1 is Et, R4a is 4-Me, R4b is 7-Me, R9 is H, R10 is H, R11 is Ph and Z is COOH is disclosed on column 25, table II. Columns 35-36 disclose pharmaceutical agents. Please note that the intended use of, such as, “preventive and/or therapeutic agent for neutrophilic inflammatory diseases”, “GPR4 antagonist”, or “preventive and/or therapeutic agent for diseases derived from

hyperfunction of GPR4" found in the preamble of some of the rejected claims is not considered a further limitation of the claim. Recitation of the intended utility into the preamble of a compound claim which can otherwise stand alone is not considered a further limitation of the claim. In re Ridden, 318 F.2d 71, 138 USPQ 112; In re Maeder, 337 F.2d 875, 143 USPQ 248; Ex parte Maxey, 177 USPQ 468 (POBA 1972); and In re Spada, 911 F.2d 705, 15 USPQ.2d 1655 (Fed. Cir. 1990). However, as can be seen by Simpson et al. (provided on the 892), asthma, which is disclosed on column 2 of the '638 patent can be considered neutrophilic. The compound disclosed on column 25, Table II corresponds to applicants instantly claimed invention, for example, wherein A1-A2-A3-A4 is N=CR3-CR4=CR5; one of R3, R4 and R5 is H and the other two are unsubstituted loweralkyl (Me); R1 is unsubstituted lower alkyl (Et); Q is unsubstituted phenylene; T is (xii) –NR11aR11b; one of R11a and R11b is unsubstituted alkyl (Me) and the other is either substituted alkyl, i.e. methyl substituted with phenyl and COOH; or substituted aralkyl, i.e. phenylalkyl substituted with COOH.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

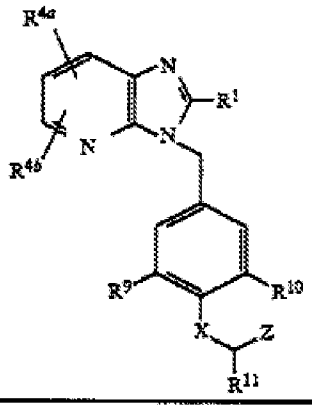
The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

Claims 17, 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,374,638.

Determining the scope and contents of the prior art:

U.S. Patent No. 5,374,638 discloses products of the formula I (column 3) which are useful for treating asthma (column 2). A particular compound:



wherein X is NMe, R1 is Et, R4a is 4-Me, R4b is 7-Me, R9 is H, R10 is H, R11 is Ph and Z is COOH is disclosed on column 25, table II. Columns 35-36 disclose pharmaceutical agents. Please note that the intended use in claim 17 of "preventive and/or therapeutic agent for neutrophilic inflammatory diseases", found in the preamble of the rejected claim is not considered a further limitation of the claim. Recitation of the intended utility into the preamble of a compound claim which can otherwise stand alone is not considered a further limitation of the claim. In re Ridden, 318 F.2d 71, 138 USPQ 112; In re Maeder, 337 F.2d 875, 143 USPQ 248; Ex parte Maxey, 177 USPQ 468 (POBA 1972); and In re Spada, 911 F.2d 705, 15 USPQ.2d 1655 (Fed. Cir. 1990). However, as can be seen by Simpson et al. (provided

on the 892), asthma, which is disclosed on column 2 of the '638 patent can be considered neutrophilic. The compound disclosed on column 25, Table II corresponds to applicants instantly claimed invention, for example, wherein A1-A2-A3-A4 is N=CR3-CR4=CR5; one of R3, R4 and R5 is H and the other two are unsubstituted loweralkyl (Me); R1 is unsubstituted lower alkyl (Et); Q is unsubstituted phenylene; T is (xii) – NR11aR11b; one of R11a and R11b is unsubstituted alkyl (Me) and the other is either substituted alkyl, i.e. methyl substituted with phenyl and COOH; or substituted aralkyl, i.e. phenylalkyl substituted with COOH.

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art claims have T or (W1 or W2) as (xii)-NR11aR11b wherein one of R11a and R11b is unsubstituted alkyl (Me) and the other is either substituted alkyl, i.e. methyl substituted with phenyl and COOH; or substituted aralkyl, i.e. phenylalkyl substituted with COOH. The instantly claimed compounds of claims 17, 41 and 42 have W1 as NHR11a or W2 as NHR11c which differs by a hydrogen versus a methyl on the nitrogen atom.

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art to prepare compounds as instantly claimed as it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that

structurally similar compounds would possess similar activity (ie., treating asthma). Additionally, it is sufficient if a reference compound is so closely related to claimed compound that a chemist would find the difference an obvious variation; thus, claims are refused where the difference is primarily the one which exists between a secondary and a tertiary amine. Ex parte Bluestone, 135 USPQ 199 (1961).

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday from 6:00am until 2:30pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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9 July 2010

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